

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1.-29. (Canceled)

30. (New) An injectable pharmaceutical product, comprising:  
an agent which comprises an insoluble carrier bound to a peptide,  
wherein:

(i) the peptide has affinity for, and is capable of non-covalent binding to, fibrinogen,  
(ii) the peptide is not fibrinogen, and  
(iii) when fibrinogen is non-covalently bound to the agent, the agent binds via said non-covalently bound fibrinogen to activated platelets in preference to inactive platelets.

31. (New) The injectable pharmaceutical product of claim 30 wherein, upon intravenous administration to a patient having a wound site which comprises activated platelets, the peptide non-covalently binds to fibrinogen and said non-covalently bound fibrinogen preferentially becomes involved in blood clot formation at the wound site.

32. (New) The injectable pharmaceutical product of claim 30 wherein the peptide comprises a sequence obtained from a fibrinogen-binding region of a platelet membrane glycoprotein, said platelet membrane glycoprotein being selected from the

group consisting of platelet membrane glycoprotein GPIIb and platelet membrane glycoprotein GPIIIa.

33. (New) The injectable pharmaceutical product of claim 32 wherein the sequence obtained from a fibrinogen-binding region of a platelet membrane glycoprotein comprises TDVNGDGRHDL (SEQ ID NO:6) or a variant thereof.

34. (New) The injectable pharmaceutical product of claim 33 wherein the variant comprises a sequence that is selected from the group consisting of T(D,E)VNG(D,E)GRH(D,E)L (SEQ ID NO:\_\_), TD(V,L)NGDGRHDL (SEQ ID NO:\_\_), TDV(N,Q)GDGRHDL (SEQ ID NO:\_\_) and TDVNGDG(R,K)HDL (SEQ ID NO:\_\_).

35. (New) The injectable pharmaceutical product of claim 30 wherein the peptide comprises TDVNGDGRHDL (SEQ ID NO:6).

36. (New) The injectable pharmaceutical product of claim 30 wherein the peptide comprises as an amino terminus the sequence Gly-(Pro/His)-Arg-Xaa (SEQ ID NO:24), wherein Xaa is any amino acid.

37. (New) The injectable pharmaceutical product of claim 30 wherein the peptide comprises as an amino terminus the sequence Gly-(Pro/His)-Arg-Xaa (SEQ ID NO:24), wherein Xaa is selected from the group consisting of Pro, Sar, Gly and Val.

38. (New) The injectable pharmaceutical product of claim 30 wherein  
(a) the peptide comprises a sequence obtained from a fibrinogen-binding region of a platelet membrane glycoprotein, said platelet membrane

glycoprotein being selected from the group consisting of platelet membrane glycoprotein GPIIb and platelet membrane glycoprotein GPIIIa, and

(b) the peptide comprises as an amino terminus the sequence Gly-(Pro/His)-Arg-Xaa (SEQ ID NO:24), wherein Xaa is any amino acid.

39. (New) The injectable pharmaceutical product of claim 38 wherein Xaa is selected from the group consisting of Pro, Sar, Gly or Val.

40. (New) The injectable pharmaceutical product of claim 30 wherein  
(a) the peptide comprises an amino acid sequence that is selected from the group consisting of TDVNGDGRHDL (SEQ ID NO:6), T(D,E)VNG(D,E)GRH(D,E)L (SEQ ID NO:\_\_), TD(V,L)NGDGRHDL (SEQ ID NO:\_\_), TDV(N,Q)GDGRHDL (SEQ ID NO:\_\_) and TDVNGDG(R,K)HDL (SEQ ID NO:\_\_), and

(b) the peptide comprises as an amino terminus the sequence Gly-(Pro/His)-Arg-Xaa (SEQ ID NO:24), wherein Xaa is any amino acid.

41. (New) The injectable pharmaceutical product of claim 40 wherein Xaa is selected from the group consisting of Pro, Sar, Gly or Val.

42. (New) The injectable pharmaceutical product according to any one of claims 30 and 32-36 wherein the peptide has from 4 to 200 amino acids.

43. (New) The injectable pharmaceutical product according to any one of claims 30 and 32-36 wherein the carrier has a size suitable to ensure transmission of the agent through the lung capillary bed.

44. (New) The injectable pharmaceutical product according to any one of claims 30 and 32-36 wherein the carrier is selected from the group consisting of a microparticle, a protein microparticle and an albumin microparticle.

45. (New) The injectable pharmaceutical product according to any one of claims 32-34 and 36 wherein the product comprises a population of carriers of which less than 2% are in excess of 6  $\mu\text{m}$  as a maximum dimension.

46. (New) The injectable pharmaceutical product according to claim 45 wherein the majority of carriers are from 2 to 4  $\mu\text{m}$  as a maximum dimension.

47. (New) The injectable pharmaceutical product according to any one of claims 32-34 and 36 wherein the peptide is bound to the carrier by a covalent bond.

48. (New) The injectable pharmaceutical product according to any one of claims 32-34 and 36 wherein the peptide is bound to the carrier by a covalent bond, wherein the peptide comprises a cysteine which comprises a -SH group and the carrier comprises a thiol reactive group, and wherein the peptide is bound to the carrier by linking the-SH group of the cysteine to the thiol reactive group on the carrier.

49. (New) An injectable pharmaceutical product, comprising:  
an agent which comprises  
(a) an insoluble carrier bound to a peptide; and  
(b) fibrinogen or a fragment or variant thereof non-covalently bound to the peptide of (a), said fibrinogen or fragment or variant thereof having an inducible platelet-aggregating activity, wherein:

- (i) the peptide of (a) has affinity for, and is capable of non-covalent binding to, fibrinogen,
- (ii) the peptide of (a) is not fibrinogen, and
- (iii) the agent binds to activated platelets in preference to inactive platelets via said non-covalently bound fibrinogen or fragment or variant thereof.

50. (New) The injectable pharmaceutical product of claim 49, wherein the peptide of (a) is selected from the group consisting of:

- (i) a peptide that comprises a sequence obtained from a fibrinogen-binding region of a platelet membrane glycoprotein, said platelet membrane glycoprotein being selected from the group consisting of platelet membrane glycoprotein GPIIb and platelet membrane glycoprotein GPIIIa,
- (ii) a peptide that comprises a sequence obtained from a fibrinogen-binding region of platelet membrane glycoprotein GPIIb or platelet membrane glycoprotein GPIIIa, said sequence comprising TDVNGDGRHDL (SEQ ID NO:6) or a variant thereof,
- (iii) a sequence that is selected from the group consisting of T(D,E)VNG(D,E)GRH(D,E)L (SEQ ID NO:\_\_), TD(V,L)NGDGRHDL (SEQ ID NO:\_\_), TDV(N,Q)GDGRHDL (SEQ ID NO:\_\_) and TDVNGDG(R,K)HDL (SEQ ID NO:\_\_),
- (iv) a peptide that comprises TDVNGDGRHDL (SEQ ID NO:6),
- (v) a peptide according to any one of (i) through (iv) which comprises as an amino terminus the sequence Gly-(Pro/His)-Arg-Xaa (SEQ ID NO:24), wherein Xaa is any amino acid, and
- (vi) a peptide according to any one of (i) through (iv) which comprises as an amino terminus the sequence Gly-(Pro/His)-Arg-Xaa (SEQ ID NO:24), wherein Xaa is selected from the group consisting of Pro, Sar, Gly and Val.

51. (New) An injectable pharmaceutical product, comprising:  
(a) an insoluble carrier;  
(b) a peptide having affinity for fibrinogen; and  
(c) fibrinogen or a variant or fragment thereof non-covalently bound to the peptide of (b),

wherein the fibrinogen or variant or fragment thereof of (c) binds to activated platelets in preference to inactive platelets.

52. (New) The injectable pharmaceutical product according to claim 51 wherein, upon intravenous administration to a patient having a wound site which comprises activated platelets, the fibrinogen or variant or fragment thereof of (c) preferentially becomes involved in blood clot formation at the wound site.

53. (New) A method of preparing an injectable pharmaceutical product, comprising:

mixing an agent with fibrinogen, or a variant or fragment thereof, under conditions and for a time sufficient to non-covalently bind the fibrinogen or variant or fragment thereof to the agent, and thereby preparing the injectable pharmaceutical product,

wherein the agent comprises an insoluble carrier bound to a peptide that is not fibrinogen, said peptide having affinity for and being capable of non-covalent binding to fibrinogen,

and wherein the agent binds to activated platelets in preference to inactive platelets via said non-covalently bound fibrinogen or fragment or variant thereof.

54. (New) The method of claim 53 further comprising at least one step that is selected from the group consisting of (a) removing unbound fibrinogen; (b) formulating the product with a pharmaceutically acceptable carrier or diluent ; (c)

diluting the product to provide a pharmaceutically acceptable unit dose; (d) sterilizing the product; and (e) ensuring product sterility throughout steps (a) to (c).

55. (New) A method of promoting haemostasis or treating thrombocytopenia in an individual, comprising administering to the individual a pharmaceutically effective dosage of an injectable product, wherein the product comprises an agent which comprises an insoluble carrier bound to a peptide, wherein:

- (i) the peptide has affinity for, and is capable of non-covalent binding to, fibrinogen,
- (ii) the peptide is not fibrinogen, and
- (iii) when fibrinogen is non-covalently bound to the agent, the agent binds to activated platelets in preference to inactive platelets.

56. (New) The method of claim 55, wherein the peptide is selected from the group consisting of:

- (i) a peptide that comprises a sequence obtained from a fibrinogen-binding region of a platelet membrane glycoprotein, said platelet membrane glycoprotein being selected from the group consisting of platelet membrane glycoprotein GPIIb and platelet membrane glycoprotein GPIIIa,
- (ii) a peptide that comprises a sequence obtained from a fibrinogen-binding region of platelet membrane glycoprotein GPIIb or platelet membrane glycoprotein GPIIIa, said sequence comprising TDVNGDGRHDL (SEQ ID NO:6) or a variant thereof,
- (iii) a sequence that is selected from the group consisting of T(D,E)VNG(D,E)GRH(D,E)L (SEQ ID NO:\_\_), TD(V,L)NGDGRHDL (SEQ ID NO:\_\_), TDV(N,Q)GDGRHDL (SEQ ID NO:\_\_) and TDVNGDG(R,K)HDL (SEQ ID NO:\_\_),
- (iv) a peptide that comprises TDVNGDGRHDL (SEQ ID NO:6),

(v) a peptide according to any one of (i) through (iv) which comprises as an amino terminus the sequence Gly-(Pro/His)-Arg-Xaa (SEQ ID NO:24), wherein Xaa is any amino acid, and

(vi) a peptide according to any one of (i) through (iv) which comprises as an amino terminus the sequence Gly-(Pro/His)-Arg-Xaa (SEQ ID NO:24), wherein Xaa is selected from the group consisting of Pro, Sar, Gly and Val.

57. (New) A method of promoting haemostasis or treating thrombocytopenia in an individual, comprising administering to the individual a pharmaceutically effective dosage of an injectable product, wherein the product comprises an agent which comprises

- (a) an insoluble carrier bound to a peptide; and
- (b) fibrinogen or a fragment or variant thereof non-covalently bound to the peptide of (a), said fibrinogen or fragment or variant thereof having an inducible platelet-aggregating activity, wherein:
  - (i) the peptide of (a) has affinity for, and is capable of non-covalent binding to, fibrinogen,
  - (ii) the peptide of (a) is not fibrinogen, and
  - (iii) the agent binds to activated platelets in preference to inactive platelets via said non-covalently bound fibrinogen or fragment or variant thereof.

58. (New) The method of claim 57, wherein the peptide of (a) is selected from the group consisting of:

- (i) a peptide that comprises a sequence obtained from a fibrinogen-binding region of a platelet membrane glycoprotein, said platelet membrane glycoprotein being selected from the group consisting of platelet membrane glycoprotein GPIIb and platelet membrane glycoprotein GPIIIa,



(ii) a peptide that comprises a sequence obtained from a fibrinogen-binding region of platelet membrane glycoprotein GPIIb or platelet membrane glycoprotein GPIIIa, said sequence comprising TDVNGDGRHDL (SEQ ID NO:6) or a variant thereof,

(iii) a sequence that is selected from the group consisting of T(D,E)VNG(D,E)GRH(D,E)L (SEQ ID NO:\_\_), TD(V,L)NGDGRHDL (SEQ ID NO:\_\_), TDV(N,Q)GDGRHDL (SEQ ID NO:\_\_) and TDVNGDG(R,K)HDL (SEQ ID NO:\_\_),

(iv) a peptide that comprises TDVNGDGRHDL (SEQ ID NO:6),

(v) a peptide according to any one of (i) through (iv) which comprises as an amino terminus the sequence Gly-(Pro/His)-Arg-Xaa (SEQ ID NO:24), wherein Xaa is any amino acid, and

(vi) a peptide according to any one of (i) through (iv) which comprises as an amino terminus the sequence Gly-(Pro/His)-Arg-Xaa (SEQ ID NO:24), wherein Xaa is selected from the group consisting of Pro, Sar, Gly and Val.

59. (New) The method of either claim 56 or claim 58 wherein the individual is selected from the group consisting of

- (i) a patient having a platelet count that is below  $400 \times 10^9/l$ ,
- (ii) a patient having a platelet count that is below  $150 \times 10^9/l$ ,
- (iii) a patient having a platelet count that is below  $10 \times 10^9/l$ ,
- (iv) a patient having an inherited or drug-induced disorder in number or function of platelets,
- (v) a patient having mechanically damaged platelets, and
- (vi) a patient having a failure in bone marrow platelet production.

Express Mail No.: EV741778575US  
International Application No.: PCT/GB2004/004235  
International Filing Date: October 7, 2004  
Preliminary Amendment

60. (New) The method of either claim 56 or claim 58 wherein the individual is a patient having a failure in bone marrow platelet production that is caused by at least one of a blood cancer, a cytotoxic chemotherapy and a radiotherapy.